

Title

The effects of dual tasking on handwriting in patients with Parkinson's disease.

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Abbreviations

DTE	Dual-Task Effect
H&Y	Hoehn & Yahr
MDS-UPDRS	Movement Disorder Society Unified Parkinson's Disease Rating Scale
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
PD	Parkinson's disease
SOS	Systematic Screening of Handwriting Difficulties
STAI	State Trait Anxiety Inventory

Abstract

Previous studies have shown that patients with Parkinson's disease (PD) experience extensive problems during dual tasking. Up to now, dual-task interference in PD has mainly been investigated in the context of gait research. However, the simultaneous performance of two different tasks is also a prerequisite to efficiently perform many other tasks in daily life, including upper limb tasks. To address this issue, this study investigated the effect of a secondary cognitive task on the performance of handwriting in patients with PD. Eighteen PD patients and 11 age-matched controls performed a writing task involving the production of repetitive loops under single- and dual-task conditions. The secondary task consisted of counting high and low tones during writing. The writing tests were performed with two amplitudes (0.6 and 1.0 cm) using a writing tablet. Results showed that dual-task performance was affected in PD patients versus controls. Dual tasking reduced writing amplitude in PD patients, but not in healthy controls ($p = 0.046$). Patients' writing size was mainly reduced during the small amplitude condition (small amplitude $p = 0.017$; large amplitude $p = 0.310$). This suggests that the control of writing at small amplitudes requires more compensational brain-processing recourses in PD and is as such less automatic than writing at large amplitudes. In addition, there was a larger dual-task effect on the secondary task in PD patients than controls ($p = 0.025$). The writing tests on the writing tablet proved highly correlated to daily life writing as measured by the 'Systematic Screening of Handwriting Difficulties' test (SOS-test) and other manual dexterity tasks, particularly during dual-task conditions. Taken together, these results provide additional insights into the motor control of handwriting and the effects of dual tasking during upper limb movements in patients with PD.

Keywords

- Parkinson's disease
- Dual tasking
- Micrographia
- Handwriting

Parkinson's disease (PD) is a common progressive neurodegenerative disorder mainly associated with a deficiency of nigrostriatal dopamine in the basal ganglia (Purves et al., 2001). Patients with PD suffer from motor problems, including bradykinesia, tremor, rigidity and postural instability, as well as cognitive and other non-motor symptoms (Jankovic, 2008). PD patients were previously shown to experience particular difficulties when performing two tasks simultaneously, known as 'dual tasking' (Benecke et al., 1986, Brown and Marsden, 1991, Castiello and Bennett, 1997, van Gemmert et al., 1998, Bond and Morris, 2000, Brown and Bennett, 2002, Woodward et al., 2002, Van Gemmert et al., 2003, Rochester et al., 2004, Pradhan et al., 2010, Proud and Morris, 2010, Wild et al., 2013). Dual tasking entails the combination of two motor tasks each aimed at different goals, for example carrying a tray while walking, or a motor task with a cognitive task, such as having a conversation while driving a car. Decreased performance during dual tasking is referred to as dual-task interference and can be ascribed to depleted attentional resources or information-processing mechanisms as well as to a loss of automaticity (Brown and Bennett, 2002, Woodward et al., 2002, Wu and Hallett, 2008). A recent review by Kelly et al. (2012) proposed several theoretical mechanisms that might explain dual-task interference during walking, such as the central capacity sharing model and the bottleneck model (Pashler, 1994, Ruthruff et al., 2001, Tombu and Jolicoeur, 2003, Lehle and Hubner, 2009). Both models propose that central attentional resources may be limited in patients with PD. When two tasks are performed simultaneously and thus compete for the same neural system, resources have to be distributed over both tasks. As a result, decreased performance or delay on one or both tasks is imminent. Functional magnetic resonance imaging (fMRI) studies partially confirmed these theoretical models, demonstrating increased brain activity in the cerebellum, premotor cortex, parietal cortex, precuneus and prefrontal cortical areas when performing automatized single motor tasks and in the bilateral precuneus during dual tasking in PD patients

as compared to healthy controls (Wu and Hallett, 2005, 2008, Wu et al., 2013). Hence, patients with PD required more brain-processing resources when performing automatic movements to overcome basal ganglia dysfunction, triggering decreased dual-task performance.

Dual-task performance in patients with PD has been investigated extensively during gait (Bond and Morris, 2000, Brown and Bennett, 2002, O'Shea et al., 2002, Rochester et al., 2004, Galletly and Brauer, 2005, Yogev et al., 2005, Brown et al., 2009, Lord et al., 2010, Pradhan et al., 2010, Wild et al., 2013). In these studies, often contradicting results were found, with some studies showing deterioration of the primary task, i.e. gait, while others mainly reported difficulties in performing the secondary task (Bloem et al., 2006, Wild et al., 2013). Dual tasking is also inherent to many other tasks in daily life, including those requiring manual dexterity. Impairments of manual dexterity, such as in handwriting, are often an early symptom of PD (Ponsen et al., 2008, Elias de Oliveira et al., 2011). It has been shown that PD patients tend to write more slowly than controls as well as progressively reduce their writing amplitude during the course of writing (Fucetola and Smith, 1997, Oliveira et al., 1997, van Gemmert et al., 1998, Van Gemmert et al., 1999, Van Gemmert et al., 2003, Ondo and Satija, 2007, Ponsen et al., 2008). This phenomenon is defined as micrographia and occurs in approximately 63% of patients with PD (McLennan et al., 1972, Wagle Shukla et al., 2012). Ponsen et al. (2008) compared handwriting performance of newly diagnosed PD patients with healthy controls, using a digitizing tablet. In contrast to controls, *de novo* PD patients showed reduced sentence length and slower writing velocities as well as a progressive reduction of letter amplitude over the course of writing. Furthermore, Broderick et al. (2009) found that when patients were required to complete a drawing task in which target size and frequency were manipulated, they produced significantly slower movements and showed less acceleration and smaller stroke sizes compared to healthy

participants. These above-mentioned handwriting problems in PD may be further deteriorated during dual-task situations and can lead to difficulties in daily life. Accordingly, it was shown that patients with PD reduce their handwriting size when the cognitive load increases, e.g. when the number of words to be written increases (Van Gemmert et al., 2001). However, up to now, only one study examined the influence of a secondary task on writing performance in PD patients. Van Gemmert et al. (1998) demonstrated decreased writing performance in PD when the secondary task consisted of orally repeating recorded digits within a 5 seconds interval. In this study, writing sequences which involved sequential task components and repositioning of the hand were tested. The purpose of the present study is to evaluate the ability to withstand dual-task interference during a basic pre-writing task in patients with PD compared to age-matched controls. In contrast to normal writing, this pre-writing task does not involve the added complexity of hand replacement, change in writing direction or the use of language and as such better allows studying the basic components of writing. As this was an unfamiliar task, we hypothesized that both patients with PD and healthy controls would show decreased performance under dual-task conditions, although we expected significantly greater dual-task interference in the patient group because of their disease-specific motor and cognitive deficits. Since handwriting is partially guided by visual input, we anticipated that the dual-task costs would have a more pronounced effect on the performance of the cognitive task than on handwriting itself. Finally, we explored the impact of different writing amplitudes on dual-task interference, as it was previously shown that writing problems in PD patients partially depend on writing size (Van Gemmert et al., 1999).

1 Experimental procedures

1.1 Participants

For this cross-sectional study, twenty nine right-handed participants were tested, including 18 PD patients (5 women, 13 men) and 11 age-matched healthy control subjects (6 women, 5 men). Patients with PD were recruited by the neurologist of the Movement Disorders Clinic at the University Hospital Leuven. Inclusion criteria for PD patients were: (i) idiopathic PD, diagnosed according to the United Kingdom PD Society Brain Bank criteria (Hughes et al., 1992) and (ii) Hoehn and Yahr (H&Y) stage I to III in the ‘on’-phase of the medication cycle (Hoehn and Yahr, 1967). The inclusion criteria for both patients and controls were: (i) being right-handed, (ii) absence of color blindness and hearing deficits and (iii) no history of depression or neurological disorders other than PD. All patients were tested in the ‘on’-phase of the medication cycle, i.e. about one hour after the last drug intake. Demographics and clinical characteristics of participants are specified in Table 1. Three patients with PD were identified as freezers as measured by the revised Freezing of Gait Questionnaire (Nieuwboer et al., 2009). Comparisons between PD and healthy controls indicated no significant differences in age, gender, cognitive status, mood and anxiety. The study design and protocol were approved by the local Ethics Committee of the KU Leuven and were in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki, 1967). After complete explanation of the study protocol, written informed consent was obtained from all participants prior to participation in the experiment.

1.2 Experimental procedure and task

Before performing the writing tests, all participants completed a clinical test-battery including the (i) Mini-Mental State Examination (MMSE) (Folstein et al., 1975) and Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), (ii) Purdue Pegboard Test (Tiffin and Asher,

1948) and (iii) Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) and State Trait Anxiety Scale (STAI) (Spielberger et al., 1983) to determine, respectively, their overall cognitive status, fine motor skills and emotional behavior. In addition, PD patients were assessed by means of the (i) Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2008) part III, (ii) H&Y scale and (iii) revised Freezing of Gait Questionnaire to assess disease severity and the occurrence of freezing of gait. As a first writing test, all participants carried out the 'Systematic Screening of Handwriting Difficulties' test (SOS-test) (Van Waelvelde et al., 2012). During this test, which is performed on paper with a regular pen, participants were instructed to copy a text during five minutes while writing as neatly and quickly as in daily life. Next, patients performed several writing tasks on a 6.4 inches custom-made writing tablet (Fujitsu Components Europe) using a stylus. The system had a sampling frequency of 200 Hz and a resolution of 32.5 μm allowing accurate registration of handwriting kinematics. A flat screen display (Flat Display Technology) provided participants with real time feedback of their writing movements. Testing took place in a quiet room where patients were seated on a height-adjustable chair in front of a table on which the writing tablet was placed. The writing tablet was incorporated into a larger frame, which provided support for the forearm and wrist (Figure 1A). Before each task, participants performed one practice trial on paper and one on the writing tablet.

Single-task writing consisted of producing a specific loop figure which reflected the essential components of writing: (i) the loop figure occurs frequently within the alphabet; and (ii) different loop sizes were used, i.e. sizes of 0.6 cm and 1.0 cm (Figure 1B and 1C resp.). The figure was developed to examine whether dual tasking would affect the basic motor sequence production inherent to writing performance without additional motor and cognitive complexity requiring

direction changes of the strokes, hand repositioning and producing meaningful language. The requested writing amplitude was indicated on the tablet by a visual reference consisting of colored target zones (grey, yellow and blue) with a bandwidth of 2 mm. For both sizes, participants were instructed to start writing within the start circle (Figure 1) and write the loops from the bottom of the blue target zone until the top of the yellow target zone returning to the bottom of the blue zone. The distance between the bottom of the blue and top of the yellow target zone was resp. 0.6 and 1.0 cm. After completion of the third loop, participants were instructed to return to the start circle via the grey target zone. Participants were encouraged to produce natural and fluent series of loops and write at a comfortable speed. Each loop disappeared from the screen at the end of the loop figure. This allowed continuous repetition of the same figure without eliciting hand repositioning movements during the whole trial lasting 27 seconds. The secondary cognitive task comprised of counting high and low pitched tones produced randomly at intervals of 3 seconds. Subjects were familiarized with the two tones prior to testing. Instructions on which tones to count were displayed on the screen before each trial. Participants were instructed to silently count either the high tones or the low tones and verbally report the total number to the examiner at the end of each trial. The tone counting task was also assessed under single-task conditions.. During dual tasking, participants received the same instructions as during single-task performance. No specific instructions regarding task prioritization were given. Three blocks of four trials were conducted for each task (i.e. tone counting task, single-task writing and dual-task writing) with a short rest interval between each trial (6 seconds). The order of the single- and dual-task trials was randomized per block for each participant.

1.3 Data processing and statistical analysis

The dependent variables, i.e. writing amplitude (% of target size) and velocity (cm/s), were defined in line with previous studies on handwriting (Oliveira et al., 1997, Lange et al., 2006, Ponsen et al., 2008). Individual up- and down-strokes were determined by calculating local minima and maxima. The amplitude of an upstroke was defined as the distance (in cm) between a local minimum and the following maximum. Similarly, the amplitude of a down-stroke was established by calculating the distance between a local maximum and the following minimum. Data from the return to the start circle, via the grey target zone, were excluded from the analysis. To compare small and large amplitudes a percentage was determined (% of target size). For each up- and down-stroke, the time to completion (s) was computed and used to calculate writing velocity (cm/s). All data were filtered at 7 Hz with a 4th order Butterworth filter and further processed using Matlab R2011b (The MathWorks) (Van Gemmert et al., 2003).

As dependent variable for the tone counting task, we expressed participants' accuracy as a percentage of correct answers per trial. To allow comparison of dual-task performance in the present task with other tasks reported in the literature, the relative effect of dual tasking was estimated by calculating the dual-task effect (DTE) for tone counting accuracy, writing amplitude and writing velocity, using the following equation (Bock, 2008, Doumas et al., 2008):

$$\text{DTE} = \frac{\text{Dual-task performance} - \text{Single-task performance}}{\text{Single-task performance}} * 100$$

Data processing for the writing task on paper (SOS-test) was performed manually by a blinded researcher. Mean writing size, writing velocity (i.e. number of letters written in 5 minutes) and total SOS-score were determined. The total SOS-score is a measure of handwriting quality and is calculated within the first five lines by evaluating the following criteria: (i) fluency of letter

formation, (ii) fluency in connections between letters, (iii) regularity of letter height, (iv) space between words and (v) straightness of the sentences (Van Waelvelde et al., 2012).

Data were analyzed using Statistica (Statistical analysis Software, version 10). All data were checked for normality of distribution and appropriate parametric or non-parametric analyses were performed. Outlier values (± 2 standard deviations) were calculated for each task and outcome parameter separately. Overall, ten outlier values were identified among the PD patients' data and seven among the data of the healthy controls. These outliers were excluded case-wise from the datasets of the corresponding variables. Mann-Whitney U tests and Chi-square tests were used to compare differences in characteristics between PD patients and healthy controls. Single- and dual-task writing performance (amplitude and velocity) were analyzed using a 2 x 2 x 2 repeated measures ANOVA design with group (PD patients, healthy controls) as between-subjects factor and task condition (single task, dual task) and size (0.6 cm, 1.0 cm) as within-subjects factors. Significant interactions were further investigated using Tukey's honest significance test as a post-hoc analysis method. Performance on the secondary cognitive task and differences in DTE between groups were analyzed using non-parametric Mann-Whitney U and Wilcoxon signed-rank tests. In addition, Spearman's rank correlations were calculated to determine the relationship between fine motor skill performance and single- and dual-task writing performance on the writing tablet. Two-sided significance levels for all tests were set at $p < 0.05$.

2 Results

2.1 Writing performance on the writing tablet

2.1.1 Amplitude

A 2 x 2 x 2 ANOVA (group x task x size) showed a significant interaction between group and task ($F_{(1, 23)} = 9.8$, $p = 0.005$). In addition, a significant main effect of size was found ($F_{(1, 23)} = 34.27$, $p < 0.0001$), indicating that participants wrote with a writing amplitude that was closer to the target amplitude in the small writing-size condition than in the large one. Simple effect analyses per task showed that PD patients had a smaller amplitude in the dual-task condition than controls ($p = 0.046$), whereas no differences between groups were found in the single-task condition (Figure 2 and Table 2). Analysis per group showed that patients had a significantly smaller amplitude during dual tasking compared to single tasking ($p = 0.002$), while this was not the case for controls (Figure 2 and Table 2). Moreover, the DTE was significantly different between patients with PD and healthy controls for the small writing-size condition ($p = 0.008$). PD patients showed a negative DTE (-4.417 ± 5.424 , Figure 3) indicating a reduction of writing amplitude under dual-task condition. In contrast, the amplitude of healthy controls marginally increased under the dual-task condition compared to the single-task condition (0.587 ± 3.757 , Figure 3). No significant differences for DTE in the large writing-size condition were found ($p = 0.639$).

2.1.2 Velocity

For writing velocity, a 2 x 2 x 2 ANOVA (group x task condition x size) revealed a significant interaction between group, task condition and size ($F_{(1, 25)} = 5.6$, $p = 0.026$). This interaction was further investigated for each size condition separately. In both the small and large writing-size condition a main effect of group was found (resp. $F_{(1, 25)} = 6.45$, $p = 0.018$; $F_{(1, 25)} = 10.11$, $p = 0.004$). This indicated that patients with PD wrote more slowly than healthy controls (Figure 4A, 4B and Table 2). For the small writing-size condition a main effect of task condition was found ($F_{(1, 25)} = 19.61$, $p < 0.0005$), showing that participants wrote slower in the dual-task condition

compared to the single-task condition. For the large writing size condition no main effect of task was found, although a trend towards significance was present ($F_{(1, 25)} = 3.9$, $p = 0.059$). Furthermore, comparing DTE in both the small and large writing-size condition showed no significant differences for velocity between patients with PD and control subjects (resp. $p = 1.000$ and $p = 0.259$, Figure 3).

2.1.3 Performance on the secondary cognitive task

Performance on the secondary (tone counting) task is shown in Figure 5. The Wilcoxon signed-rank test revealed a significant effect of task ($p = 0.00003$). Across groups, participants were less accurate in the dual-task than in the single-task condition. However, between-group analysis using a Mann-Whitney U test showed no significant differences between groups for the single- and dual-task condition (resp. $p = 0.488$ and $p = 0.112$). Furthermore, the DTE for the tone counting task significantly differed in patients and healthy controls ($p = 0.04$). The DTE was more negative for PD patients (-45.232 ± 23.044) than for control subjects (-22.278 ± 27.714), indicating that performance of PD patients decreased more in the dual-task condition than that of controls (see Figure 3).

2.2 Fine motor skills

Results of the fine motor skill tasks in PD patients and healthy controls are represented in Table 3. Mann-Whitney U tests revealed that the Purdue Pegboard Test was significantly more affected in patients with PD than controls for all sub-tasks, i.e. right-handed, left-handed, right- and left-handed and combination (resp. $p < 0.0005$, $p = 0.004$, $p < 0.0005$, $p < 0.0005$). Compared to healthy controls, PD patients showed significantly worse results for the total scores on the SOS-test ($p = 0.012$) and for the number of letters within the 5 minutes ($p = 0.006$). Moreover, PD patients scored significantly higher on the writing item (2.7) of the MDS-UPDRS

($p < 0.0005$) indicating more difficulties than healthy controls. These results imply that patients with PD experienced more problems with fine motor skills and normal writing on paper than control subjects.

2.3 Correlation analysis

Spearman's rank correlation analyses between the experimental single-task and the SOS writing scores revealed that velocities in both the small and large writing size conditions significantly correlated with number of letters written within the 5 minutes epoch on the SOS-test ($r_s = 0.627$, $p < 0.0005$ and $r_s = 0.573$, $p = 0.001$). In the single-task condition, a significant negative correlation was found between amplitude in the large writing-size condition and SOS-test total score ($r_s = -0.589$, $p = 0.001$). In addition, SOS-test writing scores correlated more strongly with the dual-task experimental conditions. More specifically, SOS-test total scores negatively correlated with amplitudes in both the small and large writing-size conditions (resp. $r_s = -0.506$, $p = 0.006$ and $r_s = -0.553$, $p = 0.003$). Significant correlations were also found between the number of letters written within the 5 minutes epoch on the SOS-test and dual-task velocities in both the small and large writing conditions (resp. $r_s = 0.645$, $p < 0.0005$ and 0.651 , $p < 0.0005$). Similar results were found for the correlations between all subtasks of the Purdue Pegboard test and single and dual task writing velocity.

3 Discussion

This study investigated the effect of a secondary cognitive task on writing performance with two different amplitudes in patients with PD. Results showed that patients with PD wrote slower than healthy controls during both single and dual tasking. Writing amplitude was more affected in PD patients than in controls in the dual-task condition. Furthermore, the results suggested that

patients with PD experienced more dual-task interference than controls on cognitive performance.

3.1 Effects of dual tasking on task performance

The hypothesis that patients with PD would experience more dual-task interference during writing than healthy controls was confirmed by this study. When participants were required to perform the cognitive tone-counting task and the writing task simultaneously, PD patients experienced more problems with maintaining the requested writing amplitude. This is in line with the study by Van Gemmert et al. (1998) who found a decreased writing amplitude in PD patients when the secondary task consisted of orally repeating recorded digits within a 5 seconds interval. In line with previous studies, PD patients wrote more slowly than healthy controls and this for both writing sizes (Van Gemmert et al., 2003, Broderick et al., 2009). Both patients and controls wrote more slowly in the dual-task condition compared to single tasking, although this decrease in velocity was only present in the small writing-size condition. Combined with the results for amplitude, these findings concur with the literature suggesting that there is a speed-accuracy trade-off in patients with PD. This meant that in the dual-task condition PD patients tended to maintain a writing speed comparable to healthy controls, at the expense of their writing amplitude (Van Gemmert et al., 1999, Van Gemmert et al., 2003, Mazzoni et al., 2007, Broderick et al., 2009). Also for the cognitive task, patients with PD were less accurate than healthy controls. However, this result should be interpreted with caution, as the interaction between task condition and group was not significant. A possible explanation for the relatively few significant differential effects for dual tasking on the cognitive task in this study might be that none of the participants showed cognitive impairment, which was previously shown to be correlated with dual-task performance (Camicioli et al., 1997, Sheridan et al., 2003).

3.2 Dual-Task interference

To further investigate dual-task interference (i.e. relative effects of dual tasking as a percentage of single-task performance), dual-task effects (DTE) were calculated for each dependent variable. Comparisons between the DTE of patients with PD and control subjects showed a significant difference for the mean DTE of writing amplitude in the small writing-size condition, but not in the large writing-size. These results may be explained by the different task requirements of small versus larger amplitude writing. The basal ganglia are important in the control of a finely graded precision grip required by handwriting (Prodoehl et al., 2009). The small amplitude movements might have needed more precision than the large ones since participants wrote the same figure within a smaller area (i.e. 0.6 cm instead of 1.0 cm). Therefore, writing at small sizes may have required more brain-processing resources in PD patients to compensate for the dysfunction in the basal ganglia-supplementary motor area circuitry. In line with the capacity models of dual tasking, limitations in neural resources might have been reached earlier when the secondary cognitive task was added to the small instead of the large amplitude task. An alternative explanation for the results may be that the production of small amplitude movements requires a different motor control circuitry. Smaller amplitude repetitions are more prone to develop rhythmical problems than larger scaled movements, such as hastening and freezing episodes (Vercruysse et al., 2012, Williams et al., 2013). Whereas the DTE was negative for writing amplitude in patients, a positive DTE was found for healthy controls. Dual-task increments are not uncommon and may point to (i) a tendency to enhance attention to the primary task, (ii) increased general levels of arousal when performing a dual-task or (iii) a beneficial temporal coupling between the two single-tasks. Interestingly, the largest DTE's in the current study were found for accuracy in the cognitive task for both PD patients and healthy controls (-45% and -22% respectively). These results suggest that the healthy controls tried to maintain their writing

performance during the dual-task condition at the expense of the tone counting accuracy, although no instruction for task prioritization was given. PD patients on the other hand, had a decreased performance on both aspects of the dual task. Similar results were obtained by Bloem et al. (2001) using the Multiple Task Test during walking. Here, it was shown that healthy controls prioritized walking during this paradigm, while PD patients tried to perform equally well on both tasks with decreased performance on both tasks as a result. This observation was also found in other dual-task studies (Bloem et al., 2006, Fuller et al., 2013). A recent study, however, contradicted these findings, as patients with PD prioritized gait at the expense of reduced cognitive performance (Wild et al., 2013). These conflicting data illustrate the task-dependency of dual task cost in the different studies.

3.3 Limitations of the study

The sample size may have compromised the statistical power and ability to detect interactions between group and task conditions. In addition, patients with PD were tested in the ‘on’-phase of the medication cycle which may have improved their performance. It has been demonstrated previously that dopaminergic medication and deep brain stimulation partially improve handwriting kinematics (Poluha et al., 1998, Bidec-Ildes et al., 2011). We used a pre-writing task to examine dual-task interference, which did not involve movement of the hand over the writing tablet. However, pre-writing performance, as tested on the writing tablet, proved highly correlated to daily life writing as measured by the SOS-test and other manual dexterity tasks, particularly during dual-task conditions. For future studies we recommend writing tasks that probe the ability to produce longer sequences and writing tasks that require variation of writing sizes to be tested in dual-task situations. Finally, this study used colored target zones to standardize the writing movement. Previous studies demonstrated improvements in bimanual and

gait performance using different cueing types even under dual-task conditions (Horstink et al., 1990, Morris et al., 1996, Baker et al., 2007, Rochester et al., 2007, Baker et al., 2008, Lohnes and Earhart, 2011). The clinical benefit of external cues has been ascribed to the recruitment of different pathways in the brain for internally- and externally-generated sequential movements (Almeida et al., 2002, Suteerawattananon et al., 2004, Lim et al., 2005, Rochester et al., 2007). Future research should therefore investigate the influence of a secondary task on both internally- and externally-generated writing sequences.

3.4 Conclusion

The current study presented data from a new dual-task paradigm to examine the influence of a cognitive task on writing in PD. The results demonstrated typical writing deficits in PD patients in the dual-task writing condition compared to age-matched controls, more specifically during small amplitude movements. PD patients were also less accurate in the cognitive task and showed an overall decrease of writing speed compared to controls. These findings provide additional insights into the motor control of writing movements in PD patients, by showing that mainly the performance in small amplitude repetitions is decreased which indicates different automatic control strategies during small and large amplitude movements. This has pointed to the necessity to conduct more study on the task constraints and particularly on the influence of providing visual references for writing when dual tasking. A better understanding of dual-task performance in PD patients is important to improve clinical assessment and to optimize treatment strategies for dual-task deficits.

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Figure Captions

Figure 1

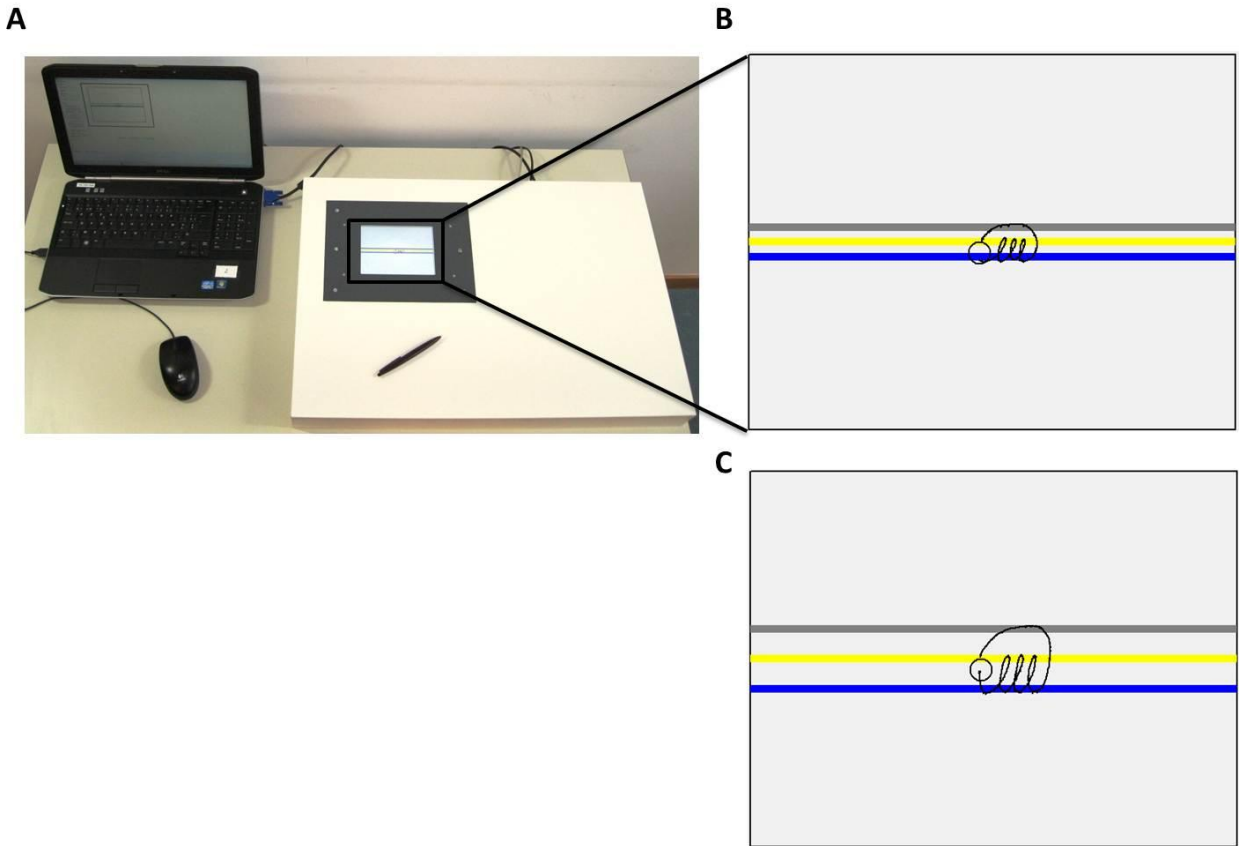


Figure 1. Experimental material and writing task. (A) The newly developed writing tablet consisted of a 6.4 inches touch sensitive screen and a display connected with a laptop. (B) Task on the writing tablet: small loop figure (0.6 cm between the bottom of the blue target zone and the top of the yellow target zone). (C) Task on the writing tablet: large loop figure (1.0 cm between the bottom of the blue target zone and the top of the yellow target zone).

Figure 2

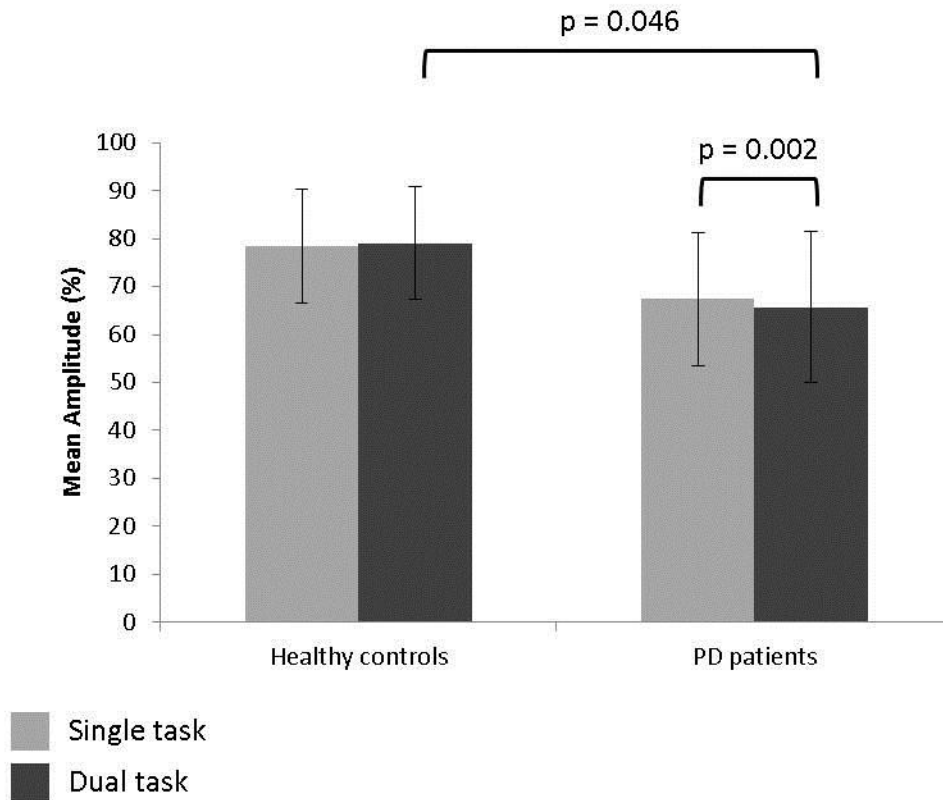


Figure 2. Mean single-task and dual-task amplitude \pm SD on the writing tablet. Dual-task amplitude is significantly different between groups ($p = 0.046$). Patients with PD show a decreased amplitude in the dual-task condition compared to the single-task condition ($p = 0.002$).

Figure 3

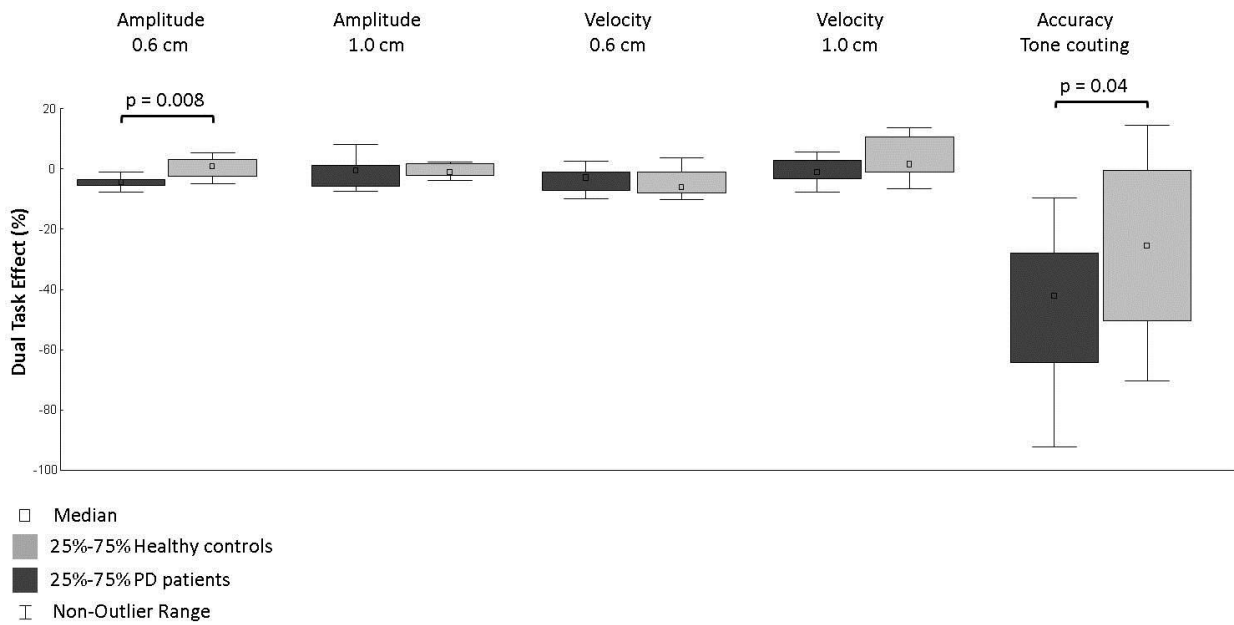


Figure 3. Positive and negative Dual-Task Effect (DTE) for PD patients and healthy controls; median and interquartile range (25%-75%). There is a significant difference between patients and healthy controls in the small amplitude condition ($p = 0.008$) and for tone counting accuracy ($p = 0.04$).

Figure 4

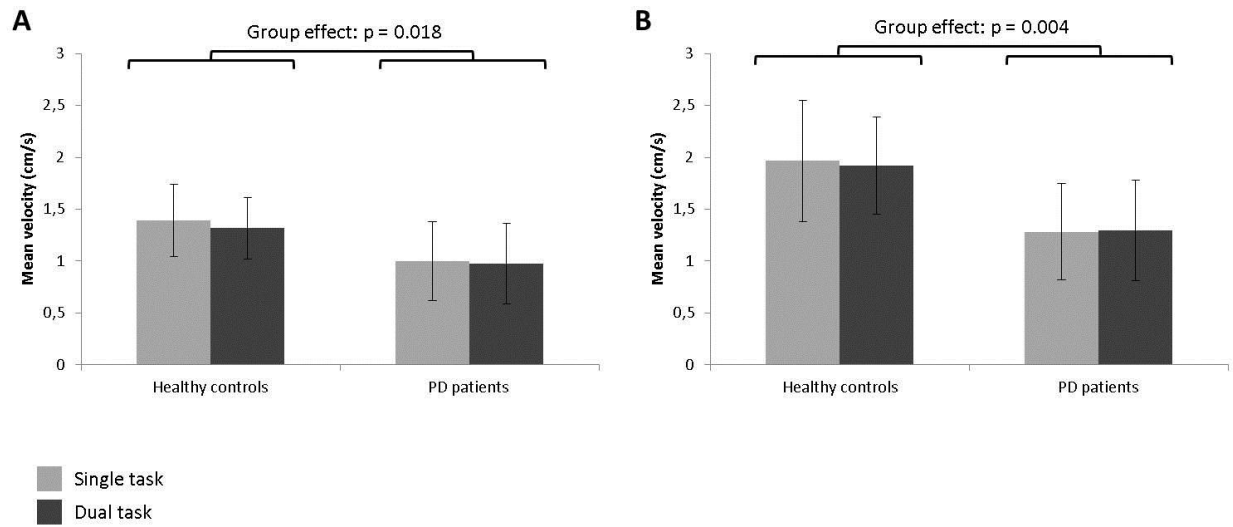


Figure 4. Mean single- and dual-task velocity \pm SD on the writing tablet. (A) Writing velocity (cm/s) in the small amplitude condition. A significant group effect ($p = 0.018$) was found, as well as a main effect of task condition ($p < 0.005$, not indicated on figure). (B) Writing velocity (cm/s) in the large amplitude condition. A main effect of group is shown ($p = 0.004$).

Figure 5

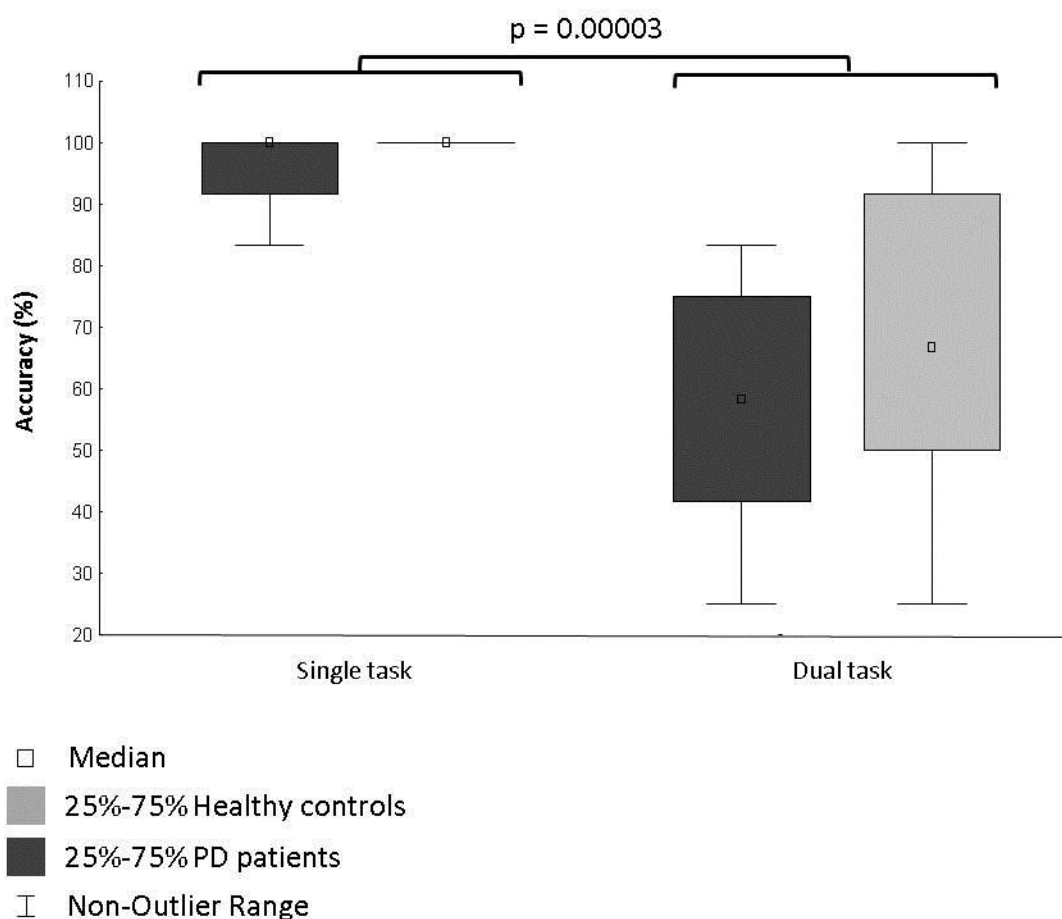


Figure 5. Single- and dual-task performance in the tone counting task for PD patients and healthy controls; median and interquartile range (25%-75%). A main effect of task condition is shown ($p = 0.00003$).

Tables

Table 1. Subject characteristics; median and interquartile range (25%-75%)

Parameter	PD patients	Controls	P-value
Age (years)	67.5 (56.8-72.0)	69 (54.0-73.0)	0.912
Gender (M/F)†	13/5	5/6	0.149
Disease duration (years)	6.5 (3.0-9.0)	-	-
MDS-UPDRS III (0-132)	25.5 (18.0-34.0)	-	-
H&Y (0-V)	2.0 (2.0-2.0)	-	-
MoCA (0-30)	27.0 (26.0-28.0)	27.0 (24.0-29.0)	0.808
MMSE (0-30)	28.0 (28.0-29.0)	29.0 (28.0-30.0)	0.161
HADS			
Anxiety subscale (0-21)	5.5 (2.0-9.0)	4.0 (1.0-6.0)	0.438
Depression subscale (0-21)	4.5 (2.0-6.0)	1.0 (1.0-5.0)	0.102
STAI (20-80)	37.0 (26.0-41.0)	27.0 (23.0-35.0)	0.111

MDS-UPDRS, Movement Disorders Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; H&Y, Hoehn and Yahr staging scale; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; HADS, Hospital Anxiety and Depression Scale; STAI, State-Trait Anxiety Inventory.

Table 2. Performance of single- and dual-task writing; mean and standard deviation

	PD patients	Controls
Writing at 0.6 cm		
Amplitude single task (%)	74.4 ± 10.2	83.1 ± 15.3
Amplitude dual task (%)	72.6 ± 11.7	84.2 ± 14.3
Velocity single task (cm/s)	1.00 ± 0.38	1.39 ± 0.35
Velocity dual task (cm/s)	0.97 ± 0.39	1.32 ± 0.30
Writing at 1.0 cm		
Amplitude single task (%)	61.5 ± 14.5	74.0 ± 10.6
Amplitude dual task (%)	59.3 ± 15.7	71.4 ± 7.7
Velocity single task (cm/s)	1.28 ± 0.47	1.97 ± 0.58
Velocity dual task (cm/s)	1.30 ± 0.48	1.92 ± 0.47

Groups significantly different at $P \leq 0.05$ (Mann-Whitney U); SOS, Systematic Screening for Handwriting Difficulties.

Table 3. Performance of fine motor skill tasks in PD patients and healthy controls; median and interquartile range (25%-75%)

	PD patients	Controls	P-value
SOS test			
Letters within 5 min	364.5 (250.5-511.8)	513.0 (493.0-603.0)	0.006*
Total score (0-10)	4.0 (1.8-5.0)	1.0 (1.0-3.0)	0.011*
Purdue Pegboard test			
Right hand	9.0 (6.0-10.3)	13.0 (11.0-14.0)	< 0.0005**
Left hand	9.0 (7.0-11.5)	13.0 (11.0-14.0)	0.004*
Bimanual	16.0 (10.0-16.0)	22.0 (18.0-24.0)	< 0.0005**
Combination	17.0 (11.8-19.3)	23.0 (20.0-30.0)	< 0.0005**

* Groups significantly different at $P \leq 0.05$ (Mann-Whitney U); SOS, Systematic Screening for Handwriting Difficulties.

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